REMARKS

Claims 1-36 are pending in the subject application. The Examiner stated that claims 1-13 and 24-36 are withdrawn from consideration. Applicants have hereinabove cancelled claims 16 and 20 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a future application. In addition, applicants have amended claims 14, 15, 17 and 21. Support for these amendments may be found inter alia in the specification as follows: claim 14: page 23, lines 30-31; page 28, lines 3-7; and claim 15: page 17, lines 18-31; page 54, lines 19-21. The remaining changes to the claims merely introduce minor grammatical and format changes.

In making these amendments, applicants neither concede the correctness of the Examiner's objection and rejections, nor abandon their right to pursue in a continuing application embodiments of the instant invention no longer claimed in this application. Applicants maintain that these amendments raise no issue of new matter, and respectfully request entry of this Amendment. Upon entry of this Amendment, claims 14, 15, 17-19 and 21-23 will be pending and under examination.

In view of the amendments to the claims and the arguments set forth below, applicants maintain that the Examiner's objection and rejections have been overcome and respectfully request that the Examiner reconsider and withdraw same.

Objection to Specification

The Examiner objected to the disclosure because it allegedly contains an embedded hyperlink and/or other form of browser-

executable code on page 26, line 29. The Examiner requires applicants to delete the embedded hyperlink and/or other form of browser-executable code (citing MPEP §608.01).

In response, applicants respectfully traverse. Nevertheless applicants without conceding the correctness of the Examiner's objection but in order to expedite prosecution of the subject application, have hereinabove amended the specification at page 26 of the subject application such that it no longer contains embedded hyperlinks and/or other form of browser-executable code. Therefore, applicants respectfully request that the Examiner reconsider and withdraw this ground of objection.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 14-23 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claims 14-23

The Examiner stated that claims 14-23 are rendered vague and indefinite in the recitation of "SML1" as the only means of identifying the protein upon which the claimed method depends. The Examiner stated that the use of a laboratory designation only to identify a protein renders the claim indefinite as other laboratories can use different designation to identify the same protein and vice versa. For example, the human spasmolytic protein is identified as SML1 (citing the abstract of Theisinger et al., (1992) *Human Genetics* 89: 681-682). Further, the Examiner stated that the application has not set

forth a definition of an Sml1 protein which could be used to determine the metes and bounds of what constitutes a Sml1 protein. The Examiner stated that amendment of the claim to recite a sequence identifier or a deposit accession number would overcome this rejection.

In response, applicants respectfully traverse. Nevertheless, without conceding the correctness of the Examiner's rejection but to expedite prosecution of the subject application, applicants have hereinabove amended claim 14. Applicants point out that newly amended claim 14 recites a sequence identifier for Sml1, i.e. SEQ ID NO: 2. In view of the above remarks, applicants maintain that claim 14, and claims 15, 17-19 and 21-23 which depend therefrom, satisfy the requirements of 35 U.S.C. §112, second paragraph and respectfully request that the Examiner reconsider and withdrawn this ground of rejection.

Claims 20-23

The Examiner stated that claims 20-23 are allegedly vague and indefinite in the recitation of "previously unknown". It is unclear what the reference point is for "previous". The Examiner stated that for purpose of examination, it will be considered as "of the priority date sought".

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 20 has been cancelled. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

Claim 15

The Examiner stated that the term "small" in claim 15 is a relative term which renders the claim indefinite. The Examiner stated that the term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In response, applicants respectfully traverse. Nevertheless, without conceding the correctness of the Examiner's rejection but to expedite prosecution of the subject application, applicants have hereinabove amended claim 15. Applicants point out that newly amended claim 15 no longer recites the term "small". In view of the above remarks, applicants maintain that claim 15 satisfies the requirements of 35 U.S.C. §112, second paragraph and respectfully request that the Examiner reconsider and withdrawn this ground of rejection.

Claim 16

The Examiner stated that claim 16 is vague and indefinite in the recitation of "a variant of a Sml1 protein". The Examiner stated that the specification fails to provide a definition for a Sml1 variant that would define the metes and bounds of the claim.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 16 has been cancelled. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 14-23 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 14-23

The Examiner stated that claims 14-23 are method claims dependent on the identity of the Sml1 protein. The Examiner stated that the specification states on page 10, lines 29-35 that an embodiment of a Sml1 protein is exemplified by SEQ ID NO: 2. The Examiner stated that the polynucleotide encoding SEQ ID NO: 2 was identified as an allele of the *S. cerevisiae* mec1 gene which can rescue the lethality of mutant Mec-1. The Examiner stated that the specification further contemplates that homologues of Sml1, such as a human, microbial, plant or insect Sml1 are other embodiments of Sml1. The Examiner stated that the specification fails to provide a written description of said homologs and further states that there are no known homologs of Sml1 (citing Zhao et al. (1998) *Molecular Cell* 2: 329-340, page 330, second column, lines 9-11). The Examiner stated that the specification states that it is likely that a homolog of Sml1 will be identified in human as the subunits of ribonucleotide reductase in yeast are closely related to those of humans (citing page 26, lines 33-36). The Examiner stated that this is not a persuasive argument because mammalian cells have two pathways of dNTP synthesis in

contrast to yeast which has a single pathway (Zhao et al., *ibid.*, page 336, second column, second full paragraph). Thus, the Examiner stated that the conservation of a Sml1 protein in mammalian cells would not be indicated as there is divergence of the pathways controlling dNTP synthesis between yeast and mammalian cells. Thus, The Examiner stated that the claims are dependent upon a genus of proteins which include unknown structural attributes. The Examiner stated that the general knowledge and skill in the art does not supplement the deficiencies of the disclosure because specific, not general guidance is what is needed. The Examiner stated that disclosure of SEQ ID NO: 2 does not anticipate this genus, because numerous structural attributes are contained within the genus. The Examiner stated that the specification does not teach what structural attributes are necessary within the homologues of SEQ ID NO: 2, thus the common attributes of the genus are not described. Further, the Examiner stated that it is noted that the Sml1 protein is encoded by an allele of mec1. The Examiner stated that the nature of alleles is that they are variant structures, and the structure of one allele does not provide information about the structure of another. The Examiner stated that one of skill in the art would conclude that applicant failed to disclose a representative number of species within the claimed genus, therefore, applicant was not in possession of the claimed genus of Sml1 proteins.

In response, applicants respectfully traverse the Examiner's rejection. First, applicants point out that Sml1 is a novel gene, not an allele of mec-1 as the Examiner states above. Applicants direct the Examiner's attention to page 23, line 29 - page 24, line 6, wherein applicants report the isolation and

characterization of *SML1*, a suppressor of *mec1* mutants. In addition, page 25, lines 7-8, recites that "the SML1 gene encodes a **novel protein** . . ." [emphasis added]. Finally, the subject specification at page 26, lines 23-30 recites the following:

> "In a genetic study, a protein in yeast was identified that interacts by binding to the largest subunit of ribonucleotide reductase (Rnr1). The binding causes negative regulation of RNR function and it is the only known protein to do so. The protein is encoded by a **novel gene** assigned the name YML058w by the yeast genomic project at Stanford. This protein has been named herein Sml1" [emphasis added].

As further evidence of the distinctness of these two genes, applicants attach hereto a copy pages from a yeast genome database which describe that Sml1 is on chromosome XIII (see Exhibit A and see also page 23, line 35 of the subject application) and MEC1 is on chromosome II (see Exhibit B) of *S. cerevisiae*. Therefore, Sml1 is not an allele of mec1.

Furthermore, with respect to homologs of Sml1, applicants direct the Examiner's attention to page 13, line 31 - page 15, line 1. Therein applicants provide a detailed description of how one of skill in the art would obtain a homolog of Sml1.

Therefore, applicants contend that the written description of the subject application does indeed satisfy the requirements of 35 U.S.C. §112, first paragraph. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims 20-23

The Examiner stated that claims 20-23 comprise the specific embodiment of "a previously unknown compound". The Examiner stated that claims 20-23 are drawn to a genus of compounds which are identified by the assay of claim 14, and were "previously unknown". The Examiner noted above that claims 20-23 are vague and indefinite without a reference point for "previous". The Examiner stated that the specification has failed to provide an adequate written description of a single "previously unknown" compound which was identified in the specification by means of the assay of claim 14. The Examiner stated that one of skill in the art would conclude that applicant failed to provide a representative number of species which would anticipate the claimed genus. Thus, the Examiner stated that Applicant was not in possession of the genus of "previously unknown" compounds.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 20 has been cancelled. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §102(b)

Nasr et al. & Sanchez et al.

The Examiner rejected claims 14 and 15 under 35 U.S.C. §102(b) as being anticipated by Nasr et al. as evidenced by Sanchez et al.

The Examiner stated that claims 14, 15 and 18 are drawn to a screening assay for identifying compounds that are capable of

reducing the division rate of a cell by altering an interaction between a ribonucleotide reductase and a Sml1 protein in the cell, which comprises: (a) contacting the cell with a compound, (b) comparing the division rate of the cell in step (a) with the division rate of the cell in the absence of the compound so as to determine whether the compound alters the interaction between the ribonucleotide reductase and the Sml1 protein of the cell, thereby reducing the cell division rate of the cell. The Examiner stated that claim 15 embodies the assay of claim 14 wherein the compound is an organic compound, a peptide, an inorganic compound, a lipid, a peptidomimetic or a small synthetic compound. The Examiner stated that claim 18 embodies the screening assay of claim 14, wherein the cell is a yeast cell, a mammalian cell, a plant cell, an insect cell or a microbe.

The Examiner stated that Nasr et al. disclose an antisense molecule to an allele of the yeast YBR1012 gene. The Examiner stated that Sanchez et al. disclose MEC1 as YBR1022. The Examiner stated that it appears that the allele of MEC1 disclosed by Nasr et al. is the same as the instant Sml1 because Sml1 is an allele of MEC1. The Examiner stated that the antisense allele disclosed by Nasr et al. would decrease the amount of Sml1 and alter the interaction between Sml1 and ribonucleotide reductase in the cell, as the resulting decrease in Sml1 levels would result in a decrease of Sml1 bound to ribonucleotide reductase.

In response, applicants respectfully traverse. Sanchez et al. describe the MEC1 gene. As discussed above, Sml1 is a novel gene, not an allele of MEC1 as the Examiner states.

Furthermore, Nasr et al. state that "the gene YBR1012 was identified during the systematic sequencing of **chromosome II** of Saccharomyces cerevisiae" [emphasis added]. Sml1 is located on **chromosome XIII** (see page 23, line 35 of the subject application and Exhibit A) [emphasis added]. Therefore, Nasr et al. does not anticipate the subject invention.

Sanchez et al.

The Examiner rejected claims 14-16 and 18 under 35 U.S.C. §102(b) as being anticipated by Sanchez et al. The Examiner stated that the specific embodiments of claims 14, 15 and 18 are set forth above. The Examiner stated that claim 16 embodies the screening assay of claim 15, wherein the peptide or the peptidomimetic is a variant of Sml1 protein or a fragment thereof. The Examiner stated that Sanchez et al. disclose that introduction of a single copy of MEC1 into a mec1 mutant dependent on overproduction for RAD53 relieves the dependency on RAD53 overproduction (citing page 357, Figure 1(B)). The Examiner stated that it is noted that claim 16 is vague and indefinite as to the metes and bounds of a "variant of a Sml1 protein". The Examiner stated that the Mec1 protein expressed as the result of the introduction of the gene encoding MEC1 is a variant of Sml1 because Sml1 is defined as an allele of Mec1.

In response, applicants respectfully traverse. Sanchez et al. describes the mec1 gene. As discussed above, Sml1 is a novel gene, not an allele of mec1. Therefore, Sanchez et al. do not anticipate the subject invention.

In view of the above remarks, applicants maintain that claims 14-16 and 18 satisfy the requirements of 35 U.S.C. §102(b).

Therefore, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §102(e)

Li et al. (U.S. Patent No. 5,767,134)

The Examiner rejected claims 14, 15, 18 and 19 under 35 U.S.C. §102(e) as being anticipated by Li et al. The Examiner stated that the specific embodiments of claims 14, 15 and 18 are set forth above. The Examiner stated that claim 19 embodies the assay of claim 14 wherein the mammalian cell is a human cell, a hamster cell, a mouse cell, a rat cell or a monkey cell.

The Examiner stated that Li et al. disclose a method of decreasing the activity of ribonucleotide reductase in a human cell comprising the administration of 3-aminopyridine-2-carboxyaldehyde thiosemicarbazone or 3-amino-4-methylpyridine-2carboxaldehyde thiosemicarbazone (citing column 1, lines 15-50 and column 2, lines 31-34 and column 4, lines 35-41). The Examiner stated that the compounds disclosed by Li et al. inhibit the activity of ribonucleotide reductase. The Examiner stated that the reference does not specifically teach that the inhibition of the ribonucleotide reductase alters the interaction between said ribonucleotide reductase and Sml1. However, the administration of the compounds disclosed by Li et al. result in inhibition of ribonucleotide reductase and a reduction in tumor growth which appears to have the same effect as the claimed alteration of the interaction between ribonucleotide reductase and Sml1 which reduces the rate of cell division. The Examiner stated that the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the

prior art does not possess the same material, structural and functional characteristics of a compound which alters the interaction between ribonucleotide reductase and Sml1 resulting in a decrease in cell division rate. The Examiner stated that in the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences.

In response, applicants respectfully traverse the Examiner's rejection. As noted by the Examiner, Li et al. do not describe the SML1 gene or protein. Li et al. therefore cannot teach a screening assay employing compounds determined to mimic the binding of Sml1 protein to ribonucleotide reductase, and thus fail to teach each and every element of the rejected claims.

Cooperman et al. (U.S. Patent No. 6,030,942)

The Examiner rejected claims 14, 15, 18 and 19 under 35 U.S.C. §102(e) as being anticipated by Cooperman et al. The Examiner stated that the specific embodiments are recited above. The Examiner stated that Cooperman et al. disclose an assay for the identification of ribonuclease reductase peptidomimetic that are able to reduce the division rate of the cell (citing column 12, lines 55-58). The Examiner stated that Cooperman et al. disclose that it is desirable to inhibit the ribonuclease reductase of a pathological cell type of a human, such as a cancer cell (citing column 14, lines 17-19), thus fulfilling the specific embodiments of claims 18 and 19 drawn to mammalian cells and human cells, respectively. The Examiner stated that Cooperman et al. do not specifically disclose that the peptidomimetic will alter the interaction between the ribonucleotide reductase and the Sml1 protein in the cell,

however, this would be inherent in the method of Cooperman et al. as the peptidomimetics would compete with ribonucleotide reductase for binding to Sml1.

In response, applicants respectfully traverse the Examiner's rejection. Cooperman et al. do not describe the SML1 gene or protein. Cooperman et al. therefore cannot teach a screening assay employing compounds determined to mimic the binding of Sml1 protein to ribonucleotide reductase, and thus fail to teach each and every element of the rejected claims.

In view of the above remarks, applicants maintain that claims 14, 15, 18 and 19 satisfy the requirements of 35 U.S.C. §102(e). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these grounds of rejection.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 14, 15, 17-19 and 21-23.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $475.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

1/30/04
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